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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/747,798	12/29/2003	George H. Yoo	INRP:104US	1871

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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/747,798	YOO, GEORGE H.	
	Examiner	Art Unit	
	Scott D. Priebe, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29,31-33 and 38-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29,31-33 and 38-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20060221*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102 & 103

Claims 1-12, 15, 18, 23-28, 33, 38-48, 51, and 54 remain rejected under 35 U.S.C. 102(a) as being anticipated by Clayman, G., Ref. C95 of the IDS filed 8/16/04, as evidenced by Oda et al. (Carcinogenesis 17(9): 2003-2008, 1996) and Flaitz et al. (Oral Oncol. 34: 448-453, 1998), and as evidenced by Recombinant DNA Advisory Committee (RAC), Minutes of Meeting March 8, 2001, U.S. Dept. of health and Human Services, for the reasons of record set forth in the Office action of 11/17/05.

Claims 1-12, 15, 18, 23-28, 33, 38-48, 51, and 54 remain rejected under 35 U.S.C. 102(b) as being anticipated by Recombinant DNA Advisory Committee (Minutes of Meeting March 8, 2001, U.S. Dept. of Health and Human Services, pages 10-12), as evidenced by Oda et al. (Carcinogenesis 17(9): 2003-2008, 1996) and Flaitz et al. (Oral Oncol. 34: 448-453, 1998), for the reasons of record set forth in the Office action of 11/17/05.

Claims 1-14, 19-29, 38-50, and 55-60 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nielsen et al., US 2001/0044420, as evidenced by Oda et al. (Carcinogenesis 17(9): 2003-2008, 1996) and Flaitz et al. (Oral Oncol. 34: 448-453, 1998) with respect to claims 1-14, 19-29, 38-50, 55-60, for the reasons of record set forth in the Office action of 11/17/05.

Claims 1-15, 18-29, 33, 38-51, 54-60 remain rejected under 35 U.S.C. 102(b) as being anticipated by El-Deiry et al., WO 99/66946, for the reasons of record set forth in the Office action of 11/17/05.

Claims 16, 17, 31, 32, 52, and 53 remain rejected under 35 U.S.C. 103(a) as being unpatentable over either Recombinant DNA Advisory Committee (Minutes of Meeting March 8, 2001, U.S. Dept. of Health and Human Services, pages 10-12), as evidenced by Oda et al. (Carcinogenesis 17(9): 2003-2008, 1996) and Flaitz et al. (Oral Oncol. 34: 448-453, 1998), as applied to claims 1-12, 15, 18, 23-28, 33, 38-48, 51, and 54 above, or El-Deiry et al., WO 99/66946, as applied to claims 1-15, 18-29, 33, 38-51, 54-60 above; and further in view of Zhang et al., WO 00/29024.

Response to Arguments

Applicant's arguments filed 2/21/06 have been fully considered but they are not persuasive.

With respect to the first three rejections set forth above, Applicant argues that Clayman, Ref. C95; RAC minutes; and Neilsen do not expressly or inherently teach treatment of papilloma virus infection. Applicant notes that the courts have held that occasional results are not inherent characteristics and that evidence of inherency must establish that the characteristic is necessarily present and cannot be based upon possibilities or probabilities. Applicant compares the instant invention to that reviewed by the court in *MEHL/Biophile*, which involved the issue of whether a

prior art method for removing tattoos with a laser inherently anticipated a method for hair removal using a laser that was aligned at a particular angle relative to a hair follicle, where the prior art did not describe the particular angle or removing hair follicles. With respect to claim 33, Applicant argues that the mouthwash described in Clayman and RAC are not inherently a douche formulated for vaginal delivery.

In response, it is agreed that none of the references explicitly states or discloses that the premalignancies or cancers being treated include cells infected with HPV. It is noted however, that page 8 of Clayman indicates that before treatment with the adenovirus, biopsies of the premalignancy are tested for the presence of HPV, which would indicate that Clayman was aware of the frequent involvement of HPV in oral dysplasia, as described in Oda and Flaitz. While it may only be probable that a premalignancy or cancer in one given individual would include HPV infected cells, the evidence presented in Oda and Flaitz show that one can be certain that in the population of individuals with oral or cervical cancer who are to be treated with the method of Clayman, RAC minutes, or Nielsen, half or most will have HPV infected cells in the premalignancy or cancer. Thus, in practicing the prior art methods for their intended purpose, one is necessarily treating HPV infected cells in most of the individuals who are the targets of the treatments. What Applicant is suggesting here, is that they be granted a monopoly on treating a majority subset of patients with oral premalignancies, i.e. those where HPV infection is involved, using a prior art method, where one of skill in the art was already aware that in most such patients the premalignancies would involve HPV infected hyperplastic cells. This is not analogous to a situation where when using a method for removing tattoos with a laser, one may occasionally happen to use the laser vertical to a hair follicle and thus ablate the follicle.

With respect to a douche formulated for vaginal delivery (claim 33), it is respectfully submitted that this is an intended-use limitation that does not distinguish the douche for vaginal delivery from the mouthwash described in Clayman and RAC. The mouthwash is a liquid that is for topical administration to the mucosa of the oral cavity, and must be mild enough not to inactivate the adenovirus. Applicant has not indicated how the prior art liquid would not also be suitable for administration to the mucosa of the vagina and cervix as a douche.

With respect to the Clayman rejection, Applicant asserts that the RAC minutes were mentioned only in the first paragraph of the rejection, and that the slides were from a presentation at Introgen, not at RAC. In response, the last paragraph of the rejection refers to the RAC minutes for the 3/8/01 meeting, and Applicant has confirmed in the Reply to the request under 37 CFR 1.105 (pages 22-23) that these slides were indeed shown at the RAC meeting on 3/8/01.

With respect to the rejection over El-Deiry, Applicant argues that p53 "homologue" as it is used in the instant specification refers to the closest homologues of human p53 found in other species, i.e. the p53 itself of other species, and that p73 is not a homologue of p53. Applicant provides an opinion declaration under 37 CFR 1.132 by Dr. Zumstein as evidence to support their arguments.

In response, what Applicant refers to in the Reply as a gene of the "same type," a gene in one species that is the corresponding gene in another species such as mouse and human p53, is termed an orthologue in the art. Genes that different yet share structurally similarity, i.e. homology, are called paralogues, e.g. p53 and p73. Paralogues are often functionally similar, but need not be. Both orthologues and paralogues are homologues, i.e. they share structural

similarity. The specification at page 14, lines 5-10, states: "[T]hroughout this application, the term "p53" is intended to refer to the exemplified p53 molecules as well as all p53 homologues from other species" (emphasis added). It does not mention "human p53," nor has Applicant indicated where the specification clearly teaches that the "exemplified p53" referred to here is human p53. The specification does not say that the homologues are limited to p53 orthologues, nor does it exclude paralogues, such as p73. It teaches "all p53 homologues," with the possible exception of paralogues of p53 from the same species as the "exemplified" p53, which the specification does not clearly identify. In the examples, the specification does not explicitly disclose that the p53 being expressed by the disclosed adenoviral vector is human p53. Consequently, one reading the specification may only speculate that the "exemplified p53" might mean human p53. Had the specification taught that p53 meant the human p53 protein or gene and all homologous p53 proteins or genes from other species, or that p53 meant human p53 and p53 from other species, one of skill would have interpreted the term p53 to mean only orthologues of p53 from any species, as Applicant contends. However, that is not what the specification teaches, Dr. Zumstein's opinion notwithstanding. Instead, it teaches that p53 includes "all p53 homologues from other species," which one of skill in the art would interpret in its broadest reasonable sense to mean both orthologues and paralogues, i.e. would include the p53-paralogue p73.

Applicant contends that the method of El-Deiry is limited to using a vector encoding human p73, but fails to indicate where such a teaching is found in the reference. Most of the description in El-Deiry refers to p73 generically, and page 4, lines 11-13, teaches as preferred coding sequences ones that encode human p73, and page 15, pages 26-30, describes sequences of

p73 orthologues from non-humans that can be used. It does teach using p53 homologues (paralogues) from other species.

Applicant also contends that p73 was not considered by one of skill in the art to be a homologue of p53, despite the fact that El-Deiry explicitly teaches that p73 is a homolog of p53. Further evidence that one of skill in the art clearly considered p73 and p53 to be homologues is provided in Kaghad et al., Cell 90: 809-819, 1997 (see entire document, especially page 810), Dr. Zumstein's opinion notwithstanding.

The Zumstein declaration under 37 CFR 1.132 filed 2/21/06 is insufficient to overcome the rejection of claims 1-29, 31-33, and 38-60 based upon El-Deiry as set forth in the last Office action for the reasons set forth above. The declaration is given little weight since it presents only the personal opinions of Dr. Zumstein on reading the specification and on the meaning of the term homolog. Also, in ¶ 6, Dr. Zumstein admits that p73 and p53 share sequence similarity, which is the only required characteristic of homologues, and functional similarity; yet states that in his opinion they are not homologues because there are also structural and functional differences. The differences are why p73 and p53 are paralogues, and not orthologues, but they are still homologues because they share structural similarity.

With respect to the rejection over either the RAC minutes or El-Deiry in view of Zhang, Applicant repeats arguments that RAC minutes or El-Deiry do not specifically teach delivery of a vector to HPV infected cells. Applicant also asserts that Zhang does not teach any of the flavorants recited in claim 17.

In response, Applicants arguments concerning the RAC minutes are addressed above. With respect to El-Deiry, this reference explicitly teaches administering the vector to HPV

infected cells, contrary to Applicants assertion. With respect to Zhang, this reference explicitly teaches peppermint flavoring, which is an oil, or oil of wintergreen (page 56, lines 28 and 29). With respect to the argument that Zhang does not teach administration to HPV infected cells, this reference was relied upon to show obviousness of including flavorants in liquids used for administration to the mouth, not for administration to HPV infected cells.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

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Primary Examiner
Art Unit 1633